

# Diverse manifestations of trichloroethylene

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**ABSTRACT** Trichloroethylene, a solvent used in a variety of industrial settings for more than 60 years, has caused adverse health effects on the central and peripheral nervous system, the skin, liver, kidney, and heart. Three men have shown relatively unusual manifestations secondary to exposure to trichloroethylene in degreasing operations in the jewellery industry. Toxic encephalopathy, hepatitis, and carpal spasm occurred among young, healthy workers. Clinical and laboratory data, including measurement of urinary trichloroacetic acid concentrations, are presented.

Trichloroethylene (TCE), a colourless, non-corrosive solvent, has been used in industrial operations since it was introduced as a degreaser in Germany during the first world war. This chlorinated aliphatic hydrocarbon replaced the flammable benzol and later found medical applications in the treatment of tic douloureux and migraine and as an anaesthetic. TCE is currently used primarily as a degreaser, although it is still sometimes used as a dry cleaning agent and as a component of some consumer products, such as spot removers and rug cleaning solutions. It also serves as a chemical intermediary in the production of paints, waxes, pesticides, and other products. Although workers are most often exposed to a mixture of solvents, the National Institute for Occupational Safety and Health (NIOSH) estimates that about 3.5 m workers are exposed at some time to TCE; about 100 000 are exposed on a full time basis.<sup>1</sup>

This paper describes three cases that represent relatively unusual manifestations of exposure to this substance.

## Health effects

The adverse health effects of TCE, which have been reviewed for two decades, include effects on the central and peripheral nervous systems, skin, liver, kidney, and heart.<sup>2-6</sup> Trigeminal neuropathy secondary to TCE exposure was first noted in 1915<sup>3</sup>; this observation led to unsuccessful attempts at curing tic douloureux with the substance.

TCE has been abused because of the euphoric effects

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that some people experience on inhaling the vapours. In one series about 4% of the workers were described as abusers<sup>7</sup>; during the second world war, some workers apparently used TCE as a substitute for alcohol.

## CASE 1

A 25 year old white man presented three days after a car accident, after which he experienced lightheadedness and dizziness while at work. For two weeks before the accident he had noticed impaired short term memory as well as "blue flashes." He was so alarmed about a loss of balance and a "spacey," lightheaded feeling that he halfheartedly suggested that he was being "drugged" by an unknown adversary. He worked with solvents and hydraulic oils in the vicinity of an annealing oven that used natural gas.

Physical examination showed a resting tremor and dysdiadochokinesia. A urinary screen for abused drugs and a preliminary assessment of liver and thyroid function gave normal results. The result of a test for carboxyhaemoglobin level, conducted to determine whether carbon monoxide from the annealing oven was the offending agent, was normal. Although the worker had suffered only a minor skull contusion without loss of consciousness, the initial clinical impression was postconcussive syndrome secondary to the car accident. The combination of cerebellar and eye findings, however, was suggestive of early multiple sclerosis, although the associated central nervous system symptoms failed to support such a diagnosis.

A short time later, the worker sought medical attention again because he had developed blurred vision and lightheadedness after cleaning a steel bar with a rag soaked with TCE. The symptoms lasted about 20 minutes. Physical examination about two

hours later showed an anxious and frightened young man who was acting differently in contrast to his customary calm demeanour. No other workers seemed to be affected, although none worked in the same work area. A 24 hour urine sample conducted that day for trichloroacetic acid later showed a concentration of 210 mg/l; the results were unavailable, however, until three weeks after sampling (figure).

Air levels of TCE measured with a portable device that used colorimetric tubes failed to indicate levels greater than 25 ppm, the lowest level recommended by any professional body, including the American Conference of Governmental Industrial Hygienists and the National Institute for Occupational Safety and Health.<sup>8</sup> Because the air levels of TCE were reported to be safe and skin absorption of TCE is not considered significant, the patient was referred to a neurologist. The evaluation included a normal CT scan, EEG, electromyography/nerve conduction velocity, and visual and somatosensory evoked response.

While awaiting the results of urine testing for TCE metabolic products, the young man showed behavioural changes obvious to both his wife and the examiner. He continued to work at his normal job.

In a follow up evaluation he complained of feeling inebriated, as though "in a daze," with a "numbness in my head." He was especially troubled by light headedness and a frequent problem that he described as seeing "flashing lights." That day at work, his job had been to submerge metal rods into a tank of TCE.

Physical examination found the anxiousness and resting tremor noted earlier as well as a profound imbalance and loss of coordination. He was advised to remain away from work. An initial report of urinary TCE metabolites confirmed the diagnosis of trichloroethylene intoxication. Urine was sampled for trichloroacetic acid that day as well. Results would not

be available for about two to three weeks but they eventually showed levels considered toxic in most previous reports (194 mg/l). Results of liver function studies were normal.

The workers compensation insurance carrier then conducted more elaborate air analysis of TCE and found the vicinity of the degreaser to be well within the recommended standard of 50 ppm (10 ppm, 7 ppm, 12 ppm). Assured that the degreaser was operating properly and that air levels of TCE were safe, the patient was approved to return to work and advised to avoid submerging his hands into the solvent tank. Shortly after returning to work, however, he developed a sense of "achey legs" and felt that his "head was screwed up" so that he felt "like punching something." The patient also described a loss of fear, claiming "nothing bothers me," and that he feared a loss of self control. He denied facial numbness but continued to have problems with his short term memory. Blood pressure was 150/100 (raised over his normotensive state). Urinary TCAA level was 15 mg/l which, according to some sources, is considered "safe." The patient was advised to stay away from work again and was then referred to the Occupational and Environmental Neurology Program of Boston University Medical Centre for an evaluation to determine the type of solvent related disorder he was experiencing.

Neurological evaluation disclosed hypalgaesia to pinprick in a mask like fashion over the face and dorsum of the hands. Deep tendon reflexes were hypoactive; there was flattening of the nasolabial fold. Neuro-ophthamological evaluation and bilateral facial latencies were normal. Neuropsychiatric evaluation showed mild to moderate cognitive changes, abnormalities associated with both exposure to solvents and depression.

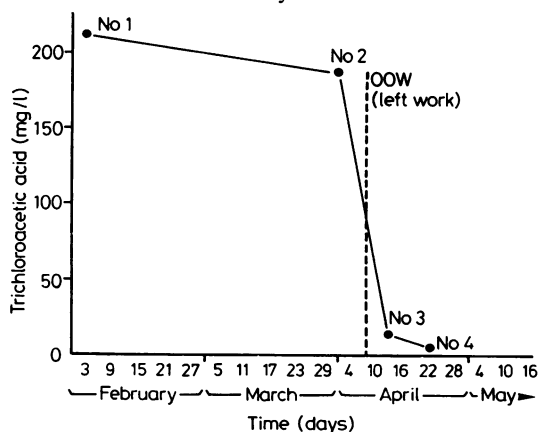
Six weeks after being removed from work, the patient returned but was transferred to an area of the plant where there was no direct or indirect exposure to TCE. He noted a pronounced reduction in feelings of "edginess" and no longer experienced the eye flashes. His short term memory improved and he no longer had the "spacey" feelings that so troubled him.

Three months later, his wife delivered a healthy seven pound boy. The patient continued to be free of symptoms noted earlier and no longer worked with TCE.

#### CASE 2

A 28 year old white man was self referred because of generalised malaise and paresthesias.

He had recently been in hospital for hepatitis of unknown aetiology and discharged. Within a week and a half of returning to work, however, he experienced numbness in his finger tips, "shooting pains in the



Case 1. Urinary (24 hour) trichloroacetic acid levels (mg/l)

hands," and loss of appetite, similar to symptoms he had noted one month before entering hospital. Because of his dissatisfaction with not learning the cause of the hepatitis and concern that "chemicals" at work might have contributed to the disorder, he sought an occupational medicine consultation.

Preliminary evaluation found no history of recent blood transfusions, dental work, or ingestion of shell fish. The man worked at a small firm (50 workers) where his major responsibilities included degreasing small metal findings for the jewellery industry. No new processes or substances had been introduced into the workplace, nor were other employees similarly affected. The only important worksite change was the recent increase in his degreasing responsibilities because a second shift had been discontinued. He had been employed at the firm in the same capacity for five years. Previously, he had worked for three years as a material handler elsewhere.

Physical examination showed psoriatic lesions over the hands and elbows. Hepatosplenomegaly or right upper quadrant tenderness was *not* detected. There was no evidence of intravenous drug abuse. Medical history was significant for psoriasis and asthma; no medication was taken other than the occasional use of Lidex cream for psoriasis.

The worker claimed he rarely drank alcohol and specifically denied any alcohol intake in the two weeks before entering hospital when he was diagnosed as suffering from acute hepatitis. He also claimed allergies to dusts, feathers, and ragweed. For six weeks before admission, he noted anorexia and tiredness, and was eventually sent to hospital because of fever, chills, and wheezing.

A review of the medical records from the hospital showed that about one week before admission he had developed an upper respiratory infection that led to coughing, wheezing, general malaise, and jaundice. Initial physical examination showed right upper quadrant tenderness and expiratory wheezes. Faecal test for occult blood was positive. Initial laboratory evaluation showed SGOT 417, LDH 1194, serum bilirubin 6.7, urine analysis +3 albumin and +1 occult blood with traces of acetone and bilirubin. White blood cell count was 6700 with a left shift (23 bands).

During the first three days in hospital, severe nausea with vomiting prompted the use of intravenous saline, which led to oedema and electrolyte imbalance (serum sodium 131-114-128). Sputum culture showed haemophilus influenza. Results from a blood test for mononucleosis and a test of the stool for ova and parasites were negative. IgM antibodies were normal. Serum bilirubin rose to 11 units. Results of tests for hepatitis surface antigen (Hbs Ag) were negative; thyroid function was normal.

Because the rise in SGOT was relatively mild for

acute viral hepatitis and common aetiologies had been eliminated, the patient was evaluated by a gastroenterologist. Calling attention to the potential for obstructive jaundice, the consultant recommended a liver scan, which showed normal size with prominence of porta hepatitis; an ultrasound of the liver, gall bladder, and pancreas was also normal. Hepatitis antibodies were not found. Eighteen days after admission, the patient was discharged with a diagnosis of acute hepatitis, aetiology pending. Serum bilirubin had decreased to 3.5 units, SGOT to 150 units, and LDH to 250; electrolytes were normal.

As part of the occupational medical evaluation, a viral screen for antibodies to toxoplasmosis and cytomegalovirus failed to show evidence of recent infection.

A visit to the worksite showed that the man worked in the basement of a small jewellery firm in a room about 30 feet long by 15 feet wide without local ventilation or windows. Trichloroethylene, used as a degreaser, was placed in an open, cylindrical container about three feet deep and a foot in diameter. The patient was responsible for dipping a metal basket of small findings into the container "hundreds of times a day." No gloves, respirator, or local ventilation were available. Other exposures included acids (sulphuric, hydrochloric) and cyanide solutions. Urinary trichloroacetic acid levels were 9 mg/l (24 hour collection) six months after the hepatitis.

### CASE 3

A 45 year old white man sought medical attention because of a "pounding headache," an inability to sleep well, and a sensation that his body felt "numb." A day earlier, he had cleaned a vapour degreaser at a jewellery firm. During the procedure, he wore an air purifying respirator and was engaged in the process for about an hour. Soon afterwards, he developed dizziness and lightheadedness of a severity that warranted leaving work early. The patient denied alcohol intake and did not smoke. Physical examination showed only slurred speech. The patient was advised of the effects of TCE and encouraged to see the safety director for an evaluation of respirator effectiveness and to have an appropriate air sampling conducted.

Three days later, however, the patient reappeared, complaining of tarry stools and a crampy feeling in his hands whenever he held an object tightly so that he would lose his grip and drop things. Physical examination showed no neurological abnormalities or evidence of tetany; however, faecal test for occult blood was positive. Serum concentrations of calcium and magnesium were within normal range. Because the patient had a history of duodenal ulcer, cimetidine and antacids, which he had not required for the preceding five years, were prescribed.

The carpal spasm persisted for six weeks until it

resolved spontaneously. The reactivated ulcer was mild in severity; the packed cell volume remained at 42%, unchanged since a test performed six months earlier. An upper gastrointestinal series with barium showed no extension of the previously noted ulcer crater.

### Discussion

These cases represent relatively unusual manifestations of TCE toxicity secondary to acute and chronic exposure. Encephalopathy characterised by impaired short term memory, a sense of inebriation, irritability, and personality changes developed from chronic, low dose exposure, primarily due to skin absorption. Trichloroacetic acid levels dropped within one week of removal from the worksite, representing a half life of TCAA of about 40 hours. Symptoms persisted, however, even at the lower levels of TCAA, a finding that suggests that other metabolic products of TCE may have contributed to some of the symptoms. Chloral hydrate, for example, an intermediary in TCE metabolism, is known to have hypnotic effects. The "achey legs" noted on several occasions suggests a solvent induced myopathy; however, without measurement of creatine phosphokinase (CPK) levels, this cannot be confirmed. Although skin absorption is not usually considered a major route of solvent exposure in man, the profound and protracted skin contact with trichloroethylene appeared to lead to the toxic effects. The importance of considering skin absorption in medical monitoring has been cited earlier.<sup>9</sup> Air measurements were repeatedly found to be within recommended levels.

Hepatitis from exposure to TCE in industrial settings is extremely rare. When TCE was used regularly as an anaesthetic, however, numerous cases were reported.<sup>10</sup> Some previously reported cases of hepatitis due to TCE are tabulated (table).<sup>11-13</sup> In five fatal cases due to inhalation of TCE one showed jaundice with

decreased urinary output.<sup>14</sup> Fatal hepatic neurosis has also occurred after massive industrial exposure.<sup>15</sup>

Liver function abnormalities have also been reported among chemical workers exposed to various solvents.<sup>16</sup> In one series 19 of 23 liver biopsies showed evidence of reactive hepatitis and fatty liver, which developed insidiously without specific symptoms.<sup>17</sup> No patient was acutely ill or had suffered an accidental exposure to solvents. The mechanism for hepatic injury of this type has been postulated as due to a direct toxic effect or hypersensitivity.<sup>18</sup> Injection of TCE has resulted in a rise in SGOT and increased neutrophilic infiltration in liver sinusoids.<sup>19</sup>

Hepatitis has also been attributed to the inhalation of spot remover that contained 45% TCE. Of ten illnesses reported secondary to sniffing spot remover, liver function abnormalities were noted in five patients, two of whom exhibited proteinuria and a rise in blood urea nitrogen.<sup>20</sup> In a review of 288 cases of industrial "poisoning" by TCE, however, only five showed evidence of hepatic signs and symptoms.<sup>21</sup>

A review of these cases of TCE associated hepatitis suggests that dose had little effect on either the development of the hepatitis or its prognosis. In addition, nine of 12 cases with hepatitis were associated with renal impairment, a finding also noted in case 2 (BUN had risen to 36 units). Liver biopsies of TCE induced hepatitis have usually shown centrilobular necrosis in both fatal and non-fatal cases.

The major causes of hepatitis are infections, types A, B, and non-A, non-B, viruses, alcohol, and drugs.<sup>22</sup> Rarer aetiologies include infectious mononucleosis, yellow fever, cytomegalovirus, other viral infections, and leptospirosis.

Although arguably extremely rare, and complicated by the concurrence of acute asthma and an upper respiratory infection, toxic insult to the liver appears to have developed secondary to TCE in case 2 for the following reasons:

(1) Other causes of hepatitis were ruled out.

### Hepatitis due to trichloroethylene

Age	Renal BUN	Creat	U/A	Liver biopsy	Exposure	Outcome
37	—	—	+ 1 ALB	Hepatic necrosis (midzonal)	6 wks of degreasing	Fatal
22	110	13.6	+ 4 Prot	Necrosis central vein area	3 days spot remover* inhalation	Fatal
15	—	—	+ 4 Prot	Granular yellow brown pigment portal areas	One year glue sniffing	Fatal
15	15	—	+ 1 Prot	Hepatic necrosis central areas	Intermittent spot remover* inhalation	Recovery
15	87	—	+ 3 Prot	Toxic hepatitis, lab biopsy not done	18 months glue sniffing intermittently followed by one week nightly of spot remover	Recovery
40	—	—	+ 1 Prot	Central lobular necrosis	Accidentally drank TCE	Fatal
18	21	—	+ 2 Prot	Centrilobular neurosis	Inhaling Carbona* (eight ounces daily for two weeks)	Recovery

\*Carbona, contains up to 70% trichloroethylene.

(2) Peripheral nervous system symptoms, not unlike that which has been reported in TCE induced neuropathy, were associated with the hepatic changes. The parasthesias appeared before clinical jaundice, returned quickly upon re-exposure to TCE, then resolved after the worker was removed from the workplace. This combination of symptoms in association with workplace exposure is strongly suggestive of a TCE induced effect.

(3) A profound change in work practices occurred, doubling the degreasing function. Scant, if any, attention was paid to good work practices or protective clothing such as impermeable gloves. Local ventilation was not present, nor had the worker been informed of the hazardous nature of TCE.

(4) The patient showed hepatorenal abnormalities similar to those noted in other cases of TCE induced hepatitis.

(5) None of the other materials with which he worked, including cyanides and acids, has been implicated as a cause of hepatitis.

A major weakness, however, in drawing this association between chronic exposure to TCE and hepatitis is the absence of a liver biopsy.

In the third case the reactivation of a duodenal ulcer that was quiescent for five years appears to represent a physical stress reaction secondary to exposure to TCE. The pathogenesis of the carpal spasm is not clear, especially since common causes, such as calcium or magnesium imbalance, could not be held accountable. Since the spasm developed a day after the acute exposure, probably a neuromuscular insult resulted from the TCE. Numerous reports have described effects on the peripheral nervous system secondary to TCE<sup>23</sup> but this case appears to be the first report of a carpal spasm. Although the peripheral nervous system impairment proved to be transient, central nervous system effects after a brief intense exposure to TCE have persisted for 18 years.<sup>24</sup>

## Conclusion

These cases point to the importance of good work practices when using potentially hazardous substances, since all the disorders described are preventable. Education in the proper handling of solvents and an effective respirator programme for tank cleaning are essential. Caution should be urged in attempting to determine absorbed dose of any substance based on air level concentrations. In addition to overlooking skin absorption these air/body concentration nomographs do not consider workload, breathing patterns, and concurrent medical conditions. Hepatitis due to TCE remains rare, although it may represent a hypersen-

sitivity reaction because of the relative independence of dose and the associated renal abnormalities.

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